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SEQUENCE LISTING

<110> HOOD, John
ELICEIRI, Brian
CHERESH, David

<120> METHODS AND COMPOSITIONS USEFUL FOR
MODULATION OF ANGIOGENESIS USING TYROSINE KINASE RAF AND RAS

<130> TSRI 710.2

<140> US 09/637,302

<141> 2000-08-11

<150> US 60/148,924

<151> 1999-08-13

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<151> 2000-07-05

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Phe Gly Phe Lys Asp Ala Val Phe Asp Gly Ser Ser Cys Ile Ser Pro
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aca ata gtt cag cag ttt ggc tat cag cgc cgg gca tca gat gat ggc 267
Thr Ile Val Gln Gln Phe Gly Tyr Gln Arg Arg Ala Ser Asp Asp Gly
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Lys Leu Thr Asp Pro Ser Lys Thr Ser Asn Thr Ile Arg Val Phe Leu
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His Asp Cys Leu Met Lys Ala Leu Lys Val Arg Gly Leu Gln Pro Glu	
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Cys Cys Ala Val Phe Arg Leu Leu His Glu His Lys Gly Lys Lys Ala	
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Arg Leu Asp Trp Asn Thr Asp Ala Ala Ser Leu Ile Gly Glu Glu Leu	
115 120 125	
caa gta gat ttc ctg gat cat gtt ccc ctc aca aca cac aac ttt gct	555
Gln Val Asp Phe Leu Asp His Val Pro Leu Thr Thr His Asn Phe Ala	
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Arg Lys Thr Phe Leu Lys Leu Ala Phe Cys Asp Ile Cys Gln Lys Phe	
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Leu Leu Asn Gly Phe Arg Cys Gln Thr Cys Gly Tyr Lys Phe His Glu	
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His Cys Ser Thr Lys Val Pro Thr Met Cys Val Asp Trp Ser Asn Ile	
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Arg Gln Leu Leu Leu Phe Pro Asn Ser Thr Ile Gly Asp Ser Gly Val	
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Pro Ala Leu Pro Ser Leu Thr Met Arg Arg Met Arg Glu Ser Val Ser	
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Arg Met Pro Val Ser Ser Gln His Arg Tyr Ser Thr Pro His Ala Phe	
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acc ttt aac acc tcc agt ccc tca tct gaa ggt tcc ctc tcc cag agg	891
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Gln Arg Ser Thr Ser Thr Pro Asn Val His Met Val Ser Thr Thr Leu	
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Ala Pro Val Ser Gly Thr Gln Glu Lys Asn Lys Ile Arg Pro Arg Gly
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Gln Arg Asp Ser Ser Tyr Tyr Trp Glu Ile Glu Ala Ser Glu Val Met
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Leu Ser Thr Arg Ile Gly Ser Gly Ser Phe Gly Thr Val Tyr Lys Gly
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Lys Trp His Gly Asp Val Ala Val Lys Ile Leu Lys Val Val Asp Pro
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Thr Pro Glu Gln Phe Gln Ala Phe Arg Asn Glu Val Ala Val Leu Arg
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Lys Thr Arg His Val Asn Ile Leu Leu Phe Met Gly Tyr Met Thr Lys
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Asp Asn Leu Ala Ile Val Thr Gln Trp Cys Glu Gly Ser Ser Leu Tyr
415 420 425 430

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Lys His Leu His Val Gln Glu Thr Lys Phe Gln Met Phe Gln Leu Ile
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Trp	Met	Ala	Pro	Glu	Val	Ile	Arg	Met	Gln	Asp	Asn	Asn	Pro	Phe	Ser		
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Thr Asp Pro Ser Lys Thr Ser Asn Thr Ile Arg Val Phe Leu Pro Asn
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Lys Gln Arg Thr Val Val Asn Val Arg Asn Gly Met Ser Leu His Asp
65 70 75 80
Cys Leu Met Lys Ala Leu Lys Val Arg Gly Leu Gln Pro Glu Cys Cys
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Ala Val Phe Arg Leu Leu His Glu His Lys Gly Lys Lys Ala Arg Leu
100 105 110
Asp Trp Asn Thr Asp Ala Ala Ser Leu Ile Gly Glu Glu Leu Gln Val
115 120 125
Asp Phe Leu Asp His Val Pro Leu Thr Thr His Asn Phe Ala Arg Lys
130 135 140
Thr Phe Leu Lys Leu Ala Phe Cys Asp Ile Cys Gln Lys Phe Leu Leu
145 150 155 160
Asn Gly Phe Arg Cys Gln Thr Cys Gly Tyr Lys Phe His Glu His Cys
165 170 175
Ser Thr Lys Val Pro Thr Met Cys Val Asp Trp Ser Asn Ile Arg Gln
180 185 190
Leu Leu Leu Phe Pro Asn Ser Thr Ile Gly Asp Ser Gly Val Pro Ala
195 200 205
Leu Pro Ser Leu Thr Met Arg Arg Met Arg Glu Ser Val Ser Arg Met
210 215 220
Pro Val Ser Ser Gln His Arg Tyr Ser Thr Pro His Ala Phe Thr Phe
225 230 235 240
Asn Thr Ser Ser Pro Ser Ser Glu Gly Ser Leu Ser Gln Arg Gln Arg
245 250 255
Ser Thr Ser Thr Pro Asn Val His Met Val Ser Thr Thr Leu Pro Val
260 265 270
Asp Ser Arg Met Ile Glu Asp Ala Ile Arg Ser His Ser Glu Ser Ala
275 280 285
Ser Pro Ser Ala Leu Ser Ser Ser Pro Asn Asn Leu Ser Pro Thr Gly
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Trp Ser Gln Pro Lys Thr Pro Val Pro Ala Gln Arg Glu Arg Ala Pro
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Val Ser Gly Thr Gln Glu Lys Asn Lys Ile Arg Pro Arg Gly Gln Arg

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Lys	Glu	Glu	Arg	Pro	Leu	Phe	Pro	Gln	Ile	Leu	Ser	Ser	Ile	Glu	Leu				
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Asp Pro Thr Ile Glu Asp Ser Tyr Arg Lys Gln Val Val Ile Asp Gly	
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Glu Thr Cys Leu Leu Asp Ile Leu Asp Thr Ala Gly Gln Glu Glu Tyr	
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agc gcc atg cgg gac cag tac atg cgc acc ggg gag ggc ttc ctg tgt	240
Ser Ala Met Arg Asp Gln Tyr Met Arg Thr Gly Glu Gly Phe Leu Cys	
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gtg ttt gcc atc aac aac acc aag tct ttt gag gac atc cac cag tac	288
Val Phe Ala Ile Asn Asn Thr Lys Ser Phe Glu Asp Ile His Gln Tyr	
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Arg Glu Gln Ile Lys Arg Val Lys Asp Ser Asp Asp Val Pro Met Val	
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50 55 60
Ser Ala Met Arg Asp Gln Tyr Met Arg Thr Gly Glu Gly Phe Leu Cys
65 70 75 80
Val Phe Ala Ile Asn Asn Thr Lys Ser Phe Glu Asp Ile His Gln Tyr
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Arg Glu Gln Ile Lys Arg Val Lys Asp Ser Asp Asp Val Pro Met Val
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Leu Val Gly Asn Lys Cys Asp Leu Ala Ala Arg Thr Val Glu Ser Arg
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Cont

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<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fusion protein

<221> CDS

<222> (1)...(2004)

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ttc aaa gat gcc gtg ttt gat ggc tcc agc tgc atc tct cct aca ata 96
Phe Lys Asp Ala Val Phe Asp Gly Ser Ser Cys Ile Ser Pro Thr Ile
20 25 30

gtt cag cag ttt ggc tat cag cgc cgg gca tca gat gat ggc aaa ctc 144
Val Gln Gln Phe Gly Tyr Gln Arg Arg Ala Ser Asp Asp Gly Lys Leu
35 40 45

aca gat cct tct aag aca agc aac act atc cgt gtt ttc ttg ccg aac 192
Thr Asp Pro Ser Lys Thr Ser Asn Thr Ile Arg Val Phe Leu Pro Asn
50 55 60

aag caa aga aca gtg gtc aat gtg cga aat gga atg agc ttg cat gac 240
Lys Gln Arg Thr Val Val Asn Val Arg Asn Gly Met Ser Leu His Asp
65 70 75 80

tgc ctt atg aaa gca ctc aag gtg agg ggc ctg caa cca gag tgc tgt 288
Cys Leu Met Lys Ala Leu Lys Val Arg Gly Leu Gln Pro Glu Cys Cys
85 90 95

gca gtg ttc aga ctt ctc cac gaa cac aaa ggt aaa aaa gca cgc tta 336
Ala Val Phe Arg Leu Leu His Glu His Lys Gly Lys Lys Ala Arg Leu
100 105 110

gat tgg aat act gat gct gcg tct ttg att gga gaa gaa ctt caa gta 384
Asp Trp Asn Thr Asp Ala Ala Ser Leu Ile Gly Glu Glu Leu Gln Val
115 120 125

gat ttc ctg gat cat gtt ccc ctc aca aca cac aac ttt gct cgg aag 432
Asp Phe Leu Asp His Val Pro Leu Thr Thr His Asn Phe Ala Arg Lys
130 135 140

acg ttc ctg aag ctt gcc ttc tgt gac atc tgt cag aaa ttc ctg ctc 480
Thr Phe Leu Lys Leu Ala Phe Cys Asp Ile Cys Gln Lys Phe Leu Leu
145 150 155 160

aat gga ttt cga tgt cag act tgt ggc tac aaa ttt cat gag cac tgt 528
Asn Gly Phe Arg Cys Gln Thr Cys Gly Tyr Lys Phe His Glu His Cys
165 170 175

agc acc aaa gta cct act atg tgt gtg gac tgg agt aac atc aga caa 576

Ser	Thr	Lys	Val	Pro	Thr	Met	Cys	Val	Asp	Trp	Ser	Asn	Ile	Arg	Gln	
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Leu	Leu	Leu	Phe	Pro	Asn	Ser	Thr	Ile	Gly	Asp	Ser	Gly	Val	Pro	Ala	
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cta	cct	tct	ttg	act	atg	cgt	cgt	atg	cga	gag	tct	gtt	tcc	agg	atg	672
Leu	Pro	Ser	Leu	Thr	Met	Arg	Arg	Met	Arg	Glu	Ser	Val	Ser	Arg	Met	
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cct	gtt	agt	tct	cag	cac	aga	tat	tct	aca	cct	cac	gcc	ttc	acc	ttt	720
Pro	Val	Ser	Ser	Gln	His	Arg	Tyr	Ser	Thr	Pro	His	Ala	Phe	Thr	Phe	
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aac	acc	tcc	agt	ccc	tca	tct	gaa	ggg	tcc	ctc	tcc	cag	agg	cag	agg	768
Asn	Thr	Ser	Ser	Pro	Ser	Ser	Glu	Gly	Ser	Leu	Ser	Gln	Arg	Gln	Arg	
				245				250					255			
tcg	aca	tcc	aca	cct	aat	gtc	cac	atg	gtc	agc	acc	acg	ctg	cct	gtg	816
Ser	Thr	Ser	Thr	Pro	Asn	Val	His	Met	Val	Ser	Thr	Thr	Leu	Pro	Val	
			260					265					270			
gac	agc	agg	atg	att	gag	gat	gca	att	cga	agt	cac	agc	gaa	tca	gcc	864
Asp	Ser	Arg	Met	Ile	Glu	Asp	Ala	Ile	Arg	Ser	His	Ser	Glu	Ser	Ala	
		275					280					285				
tca	cct	tca	gcc	ctg	tcc	agt	agc	ccc	aac	aat	ctg	agc	cca	aca	ggc	912
Ser	Pro	Ser	Ala	Leu	Ser	Ser	Ser	Pro	Asn	Asn	Leu	Ser	Pro	Thr	Gly	
	290					295					300					
tg	tca	cag	ccg	aaa	acc	ccc	gtg	cca	gca	caa	aga	gag	cgg	gca	cca	960
Trp	Ser	Gln	Pro	Lys	Thr	Pro	Val	Pro	Ala	Gln	Arg	Glu	Arg	Ala	Pro	
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gta	tct	ggg	acc	cag	gag	aaa	aac	aaa	att	agg	cct	cgt	gga	cag	aga	1008
Val	Ser	Gly	Thr	Gln	Glu	Lys	Asn	Lys	Ile	Arg	Pro	Arg	Gly	Gln	Arg	
				325				330					335			
gat	tca	agc	tat	tat	tgg	gaa	ata	gaa	gcc	agt	gaa	gtg	atg	ctg	tcc	1056
Asp	Ser	Ser	Tyr	Tyr	Trp	Glu	Ile	Glu	Ala	Ser	Glu	Val	Met	Leu	Ser	
			340					345				350				
act	cgg	att	ggg	tca	ggc	tct	ttt	gga	act	gtt	tat	aag	ggg	aaa	tgg	1104
Thr	Arg	Ile	Gly	Ser	Gly	Ser	Phe	Gly	Thr	Val	Tyr	Lys	Gly	Lys	Trp	
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cac	gga	gat	gtt	gca	gta	aag	atc	cta	aag	gtt	gtc	gac	cca	acc	cca	1152
His	Gly	Asp	Val	Ala	Val	Lys	Ile	Leu	Lys	Val	Val	Asp	Pro	Thr	Pro	
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gag	caa	ttc	cag	gcc	ttc	agg	aat	gag	gtg	gct	gtt	ctg	cgc	aaa	aca	1200
Glu	Gln	Phe	Gln	Ala	Phe	Arg	Asn	Glu	Val	Ala	Val	Leu	Arg	Lys	Thr	

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385	390	395	400	
cgg cat gtg aac att ctg ctt ttc atg ggg tac atg aca aag gac aac				1248
Arg His Val Asn Ile Leu Leu Phe Met Gly Tyr Met Thr Lys Asp Asn				
405		410	415	
ctg gca att gtg acc cag tgg tgc gag ggc agc agc ctc tac aaa cac				1296
Leu Ala Ile Val Thr Gln Trp Cys Glu Gly Ser Ser Leu Tyr Lys His				
420		425	430	
ctg cat gtc cag gag acc aag ttt cag atg ttc cag cta att gac att				1344
Leu His Val Gln Glu Thr Lys Phe Gln Met Phe Gln Leu Ile Asp Ile				
435		440	445	
gcc cgg cag acg gct cag gga atg gac tat ttg cat gca aag aac atc				1392
Ala Arg Gln Thr Ala Gln Gly Met Asp Tyr Leu His Ala Lys Asn Ile				
450		455	460	
atc cat aga gac atg aaa tcc aac aat ata ttt ctc cat gaa ggc tta				1440
Ile His Arg Asp Met Lys Ser Asn Asn Ile Phe Leu His Glu Gly Leu				
465		470	475	480
aca gtg aaa att gga gat ttt ggt ttg gca aca gta aag tca cgc tgg				1488
Thr Val Lys Ile Gly Asp Phe Gly Leu Ala Thr Val Lys Ser Arg Trp				
485		490	495	
agt ggt tct cag cag gtt gaa caa cct act ggc tct gtc ctc tgg atg				1536
Ser Gly Ser Gln Gln Val Glu Gln Pro Thr Gly Ser Val Leu Trp Met				
500		505	510	
gcc cca gag gtg atc cga atg cag gat aac aac cca ttc agt ttc cag				1584
Ala Pro Glu Val Ile Arg Met Gln Asp Asn Asn Pro Phe Ser Phe Gln				
515		520	525	
tcg gat gtc tac tcc tat ggc atc gta ttg tat gaa ctg atg acg ggg				1632
Ser Asp Val Tyr Ser Tyr Gly Ile Val Leu Tyr Glu Leu Met Thr Gly				
530		535	540	
gag ctt cct tat tct cac atc aac aac cga gat cag atc atc ttc atg				1680
Glu Leu Pro Tyr Ser His Ile Asn Asn Arg Asp Gln Ile Ile Phe Met				
545		550	555	560
gtg ggc cga gga tat gcc tcc cca gat ctt agt aag cta tat aag aac				1728
Val Gly Arg Gly Tyr Ala Ser Pro Asp Leu Ser Lys Leu Tyr Lys Asn				
565		570	575	
tgc ccc aaa gca atg aag agg ctg gta gct gac tgt gtg aag aaa gta				1776
Cys Pro Lys Ala Met Lys Arg Leu Val Ala Asp Cys Val Lys Lys Val				
580		585	590	
aag gaa gag agg cct ctt ttt ccc cag atc ctg tct tcc att gag ctg				1824
Lys Glu Glu Arg Pro Leu Phe Pro Gln Ile Leu Ser Ser Ile Glu Leu				
595		600	605	

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Cont.

ctc caa cac tct cta ccg aag atc aac cgg agc gct tcc gag cca tcc 1872
Leu Gln His Ser Leu Pro Lys Ile Asn Arg Ser Ala Ser Glu Pro Ser
610 615 620

ttg cat cgg gca gcc cac act gag gat atc aat gct tgc acg ctg acc 1920
Leu His Arg Ala Ala His Thr Glu Asp Ile Asn Ala Cys Thr Leu Thr
625 630 635 640

acg tcc ccg agg ctg cct gtc ttc tac tcg ttc ctg ccg ttc ttc ttc 1968
Thr Ser Pro Arg Leu Pro Val Phe Tyr Ser Phe Leu Pro Phe Phe Phe
645 650 655

ttc ttc ttc tcg ttc tgt ttc acg cct agt aca ttc 2004
Phe Phe Phe Ser Phe Cys Phe Thr Pro Ser Thr Phe
660 665

<210> 7

<211> 668

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fusion protein

<400> 7

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Val Gln Gln Phe Gly Tyr Gln Arg Arg Ala Ser Asp Asp Gly Lys Leu
35 40 45
Thr Asp Pro Ser Lys Thr Ser Asn Thr Ile Arg Val Phe Leu Pro Asn
50 55 60
Lys Gln Arg Thr Val Val Asn Val Arg Asn Gly Met Ser Leu His Asp
65 70 75 80
Cys Leu Met Lys Ala Leu Lys Val Arg Gly Leu Gln Pro Glu Cys Cys
85 90 95
Ala Val Phe Arg Leu Leu His Glu His Lys Gly Lys Lys Ala Arg Leu
100 105 110
Asp Trp Asn Thr Asp Ala Ala Ser Leu Ile Gly Glu Glu Leu Gln Val
115 120 125
Asp Phe Leu Asp His Val Pro Leu Thr Thr His Asn Phe Ala Arg Lys
130 135 140
Thr Phe Leu Lys Leu Ala Phe Cys Asp Ile Cys Gln Lys Phe Leu Leu
145 150 155 160
Asn Gly Phe Arg Cys Gln Thr Cys Gly Tyr Lys Phe His Glu His Cys
165 170 175
Ser Thr Lys Val Pro Thr Met Cys Val Asp Trp Ser Asn Ile Arg Gln
180 185 190
Leu Leu Leu Phe Pro Asn Ser Thr Ile Gly Asp Ser Gly Val Pro Ala
195 200 205

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Leu	Pro	Ser	Leu	Thr	Met	Arg	Arg	Met	Arg	Glu	Ser	Val	Ser	Arg	Met
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225					230					235					240
Asn	Thr	Ser	Ser	Pro	Ser	Ser	Glu	Gly	Ser	Leu	Ser	Gln	Arg	Gln	Arg
				245					250					255	
Ser	Thr	Ser	Thr	Pro	Asn	Val	His	Met	Val	Ser	Thr	Thr	Leu	Pro	Val
			260					265					270		
Asp	Ser	Arg	Met	Ile	Glu	Asp	Ala	Ile	Arg	Ser	His	Ser	Glu	Ser	Ala
		275					280					285			
Ser	Pro	Ser	Ala	Leu	Ser	Ser	Ser	Pro	Asn	Asn	Leu	Ser	Pro	Thr	Gly
	290					295				300					
Trp	Ser	Gln	Pro	Lys	Thr	Pro	Val	Pro	Ala	Gln	Arg	Glu	Arg	Ala	Pro
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Val	Ser	Gly	Thr	Gln	Glu	Lys	Asn	Lys	Ile	Arg	Pro	Arg	Gly	Gln	Arg
				325					330					335	
Asp	Ser	Ser	Tyr	Trp	Glu	Ile	Glu	Ala	Ser	Glu	Val	Met	Leu	Ser	
			340				345					350			
Thr	Arg	Ile	Gly	Ser	Gly	Ser	Phe	Gly	Thr	Val	Tyr	Lys	Gly	Lys	Trp
		355					360					365			
His	Gly	Asp	Val	Ala	Val	Lys	Ile	Leu	Lys	Val	Val	Asp	Pro	Thr	Pro
	370					375				380					
Glu	Gln	Phe	Gln	Ala	Phe	Arg	Asn	Glu	Val	Ala	Val	Leu	Arg	Lys	Thr
385					390					395					400
Arg	His	Val	Asn	Ile	Leu	Leu	Phe	Met	Gly	Tyr	Met	Thr	Lys	Asp	Asn
			405						410					415	
Leu	Ala	Ile	Val	Thr	Gln	Trp	Cys	Glu	Gly	Ser	Ser	Leu	Tyr	Lys	His
		420						425					430		
Leu	His	Val	Gln	Glu	Thr	Lys	Phe	Gln	Met	Phe	Gln	Leu	Ile	Asp	Ile
	435						440					445			
Ala	Arg	Gln	Thr	Ala	Gln	Gly	Met	Asp	Tyr	Leu	His	Ala	Lys	Asn	Ile
	450					455					460				
Ile	His	Arg	Asp	Met	Lys	Ser	Asn	Asn	Ile	Phe	Leu	His	Glu	Gly	Leu
465				470						475					480
Thr	Val	Lys	Ile	Gly	Asp	Phe	Gly	Leu	Ala	Thr	Val	Lys	Ser	Arg	Trp
			485					490						495	
Ser	Gly	Ser	Gln	Gln	Val	Glu	Gln	Pro	Thr	Gly	Ser	Val	Leu	Trp	Met
			500					505					510		
Ala	Pro	Glu	Val	Ile	Arg	Met	Gln	Asp	Asn	Asn	Pro	Phe	Ser	Phe	Gln
		515					520					525			
Ser	Asp	Val	Tyr	Ser	Tyr	Gly	Ile	Val	Leu	Tyr	Glu	Leu	Met	Thr	Gly
	530					535					540				
Glu	Leu	Pro	Tyr	Ser	His	Ile	Asn	Asn	Arg	Asp	Gln	Ile	Ile	Phe	Met
545					550					555					560
Val	Gly	Arg	Gly	Tyr	Ala	Ser	Pro	Asp	Leu	Ser	Lys	Leu	Tyr	Lys	Asn
				565					570					575	
Cys	Pro	Lys	Ala	Met	Lys	Arg	Leu	Val	Ala	Asp	Cys	Val	Lys	Lys	Val
			580					585					590		
Lys	Glu	Glu	Arg	Pro	Leu	Phe	Pro	Gln	Ile	Leu	Ser	Ser	Ile	Glu	Leu
	595						600					605			
Leu	Gln	His	Ser	Leu	Pro	Lys	Ile	Asn	Arg	Ser	Ala	Ser	Glu	Pro	Ser
	610					615					620				
Leu	His	Arg	Ala	Ala	His	Thr	Glu	Asp	Ile	Asn	Ala	Cys	Thr	Leu	Thr

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625 630 635 640
Thr Ser Pro Arg Leu Pro Val Phe Tyr Ser Phe Leu Pro Phe Phe Phe
645 650 655
Phe Phe Phe Ser Phe Cys Phe Thr Pro Ser Thr Phe
660 665
